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| APPLICATION NO.  | FILING DATE | FIRST NAMED INVENTOR | ATTORNEY DOCKET NO. | CONFIRMATION NO. |
|--|-------------|----------------------|---------------------|------------------|
| 09/520,004   | 03/06/2000  | John Paul Maye       | 046436-5016         | 7731             |
| 21874 7590 11/16/2009<br>EDWARDS ANGELL PALMER & DODGE LLP<br>P.O. BOX 55874<br>BOSTON, MA 02205 |             |                      |                     |                  |
| EXAMINER   |             |                      |                     |                  |
| STULIL, VERA   |             |                      |                     |                  |
| ART UNIT   |             | PAPER NUMBER         |                     |                  |
| 1794   |             |                      |                     |                  |
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**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

# Office Action Summary

**Application No.**

09/520,004

**Applicant(s)**

MAYE ET AL.

**Examiner**

VERA STULII

**Art Unit**

1794

**Period for Reply** -- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 11 June 2009.
- 2a) ☒ This action is **FINAL**. 2b) ☐ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 2-21 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 2-21 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.
- Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).
- Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All b) ☐ Some \* c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
  2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
  3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- 1) ☐ Notice of References Cited (PTO-892)
- 2) ☐ Notice of Draftperson's Patent Drawing Review (PTO-948)
- 3) ☐ Information Disclosure Statement(s) (PTO/SB/08)
- 4) ☐ Interview Summary (PTO-413)
- 5) ☐ Notice of Informal Patent Application
- 6) ☐ Other: \_\_\_\_\_

**DETAILED ACTION**

***Claim Rejections - 35 USC § 103***

The text of those sections of Title 35, U.S. Code not included in this action can be found in a prior Office action.

**Claims 2-6, 8-11, 14-15 and 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Todd, Jr. et al. (US 5,082,975) for the reasons given in the Final Office action mailed March 19, 2008 and Non-Final Office action mailed December 11, 2008.**

In regard to the newly added limitation in claims 2 and 14, it is noted that in regard to the yeast growing in the presence of air, it was well known in the art that oxygen is one of the required components of the yeast growing media, and that aerobic growth of yeast is a standard practice in the art. It is further noted that alcoholic fermentation under anaerobic conditions where alcohol is formed from sugar was a well established fact in the art as well.

**Claims 7 and 16-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Todd, Jr. et al. (US 5,082,975) in view of Simpson (Synergism Between Hop Resins and Phosphoric Acid And Its Relevance To The Acid Washing of Yeast) for the reasons given in the Final Office action mailed March 19, 2008 and Non-Final Office action mailed December 11, 2008.**

**Claims 12-13 are rejected under 35 U.S.C. 103(a) as being unpatentable over Todd, Jr. et al. (US 5,082,975) in view of Simpson (Synergism Between Hop Resins and Phosphoric Acid And Its Relevance To The Acid Washing of Yeast)**

**and further in view of Todd, Jr. (US 4,002,683) for the reasons given in the Final Office action mailed March 19, 2008 and Non-Final Office action mailed December 11, 2008.**

***Response to Arguments***

Applicant's arguments filed 06/11/2009 have been fully considered but they are not persuasive.

On page 7 of the Reply to the Office action mailed 12/11/2008 filed 06/11/2009, Applicant states that:

Todd is directed towards a synthetic method of converting beta acids into reduced beta acids. Todd indicates that beta acids may be added to a yeast culture to inhibit bacterial growth (column 3, lines 7-8), and that the reduced beta acids may be used in the brewhouse (column 8, lines 5-10). Additionally, Todd discloses that treatment of a sugar solution inoculated with yeast, with an alkaline beta hop acid solution in water, did NOT inhibit fermentation.

In response to this argument, it is noted that Todd, Jr. et al. disclose synthesis of hydrogenated purified beta acid (hexahydrolupulone) and its use as a selective inhibitor of cell growth (Col. 2 lines 33-41, Col. 3 lines 7-20), "the addition of hexahydrolupulone to a yeast culture to inhibit the growth of Lactobacillus therein" (Col. 3 lines 7-8), "the inhibition of a Lactobacillus microorganism in the presence of yeast without inhibiting growth of the yeast by the application of a Lactobacillus-inhibiting amount of hexahydrolupulone thereto" (Col. 3 lines 9-11).

In response to applicant's argument that the references fail to show certain features of applicant's invention (page 7 of the Reply), it is noted that the features upon which applicant relies (i.e., avoiding/minimizing fermentation, activity of the yeast) are

not recited in the rejected claim(s). Although the claims are interpreted in light of the specification, limitations from the specification are not read into the claims. See *In re Van Geuns*, 988 F.2d 1181, 26 USPQ2d 1057 (Fed. Cir. 1993).

On page 6 of the Reply, applicant states that "[t]he text of Todd is therefore directed towards the treatment of a sugar solution, yeast, and hexahydrolupulone, for fermentation. This statement in Todd merely relates to fermentation and provides no teaching whatsoever in regards to yeast propagation. Yeast propagation is nowhere alluded to in Todd." In response to applicant's arguments against the references individually, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Todd, Jr. et al. disclose:

- hydrogenated purified beta acid (hexahydrolupulone) and its use as a selective inhibitor of cell growth (Col. 2 lines 33-41, Col. 3 lines 7-20);
- "the addition of hexahydrolupulone to a yeast culture to inhibit the growth of *Lactobacillus* therein" (Col. 3 lines 7-8);
- "the inhibition of a *Lactobacillus* microorganism in the presence of yeast without inhibiting growth of the yeast by the application of a *Lactobacillus*-inhibiting amount of hexahydrolupulone thereto" (Col. 3 lines 9-11).
- "the selective inhibition of one microorganism in the presence of another by the application of an amount of hexahydrolupulone which is inhibitory as to the one microorganism but not the other" (Col. 3 lines 16-19).

Simpson discloses:

- "compounds derived from hops" protect beer against spoilage by lactic acid bacteria (p. 405);
- (-)-humulone (an alpha acid), colupulone (a beta-acid), trans-isohumulone (an iso-alpha acid), and trans-humulonic acid (a hydrolysis product of (-)-humulone and isohumulone) as inhibiting agents;
- MIC (minimal inhibitory concentration) is the smallest concentration of a substance that inhibits growth of the test organism in a given time (p.406, Fig. 2);
- antibacterial activity of hop bitter acids was increased by monovalent cations (such as K, Na, Rb) (p.406);
- "most strains of lactic acid bacteria are inhibited by 10-15  $\mu$ M [3.5-5.3 ppm] trans-isohumulone" (p.410).

As stated above, Since Todd, Jr. et al disclose use of hexahydrolupulone to inhibit the growth of Lactobacillus in the brewhouse (alcohol production) and in other fermentation processes (Col. 8 lines 8-12), and since it was well known in the art to use hop acids (resins) extracts for preparation of yeast fermentation mash in alcohol (ethanol) production, one of the ordinary skill in the art would have been motivated to modify disclosure of Todd, Jr. et al and to use hop acids extract in ethanol (alcohol) production at any stage of the ethanol production where inhibiting of bacteria is required. One of ordinary skill in the art would have been motivated to use hop acids solutions in production of ethanol to inhibit growth of Lactic acid bacteria, since it was

well known in the art to use hop acids (resins) extracts for preparation of yeast fermentation mash in alcohol (ethanol) production for antibacterial purposes. One of ordinary skill in the art would have been motivated to add hop acids solutions to the yeast growing tank, and then to transfer the mixture to the fermentation vessel, since Todd, Jr. et al. disclose "the addition of hexahydrolupulone to a yeast culture to inhibit the growth of *Lactobacillus* therein" (Col. 3 lines 7-8). The specific conditions of yeast growing (such as addition of air) would not impart any patentable distinction.

In response to the argument, regarding the growth of yeast under aerobic conditions, it is noted that it was well known in the art that oxygen is one of the required components of the yeast growing media, and that aerobic growth of yeast is a standard practice in the art.

In response to applicant's arguments against the references individually (Simpson and Todd'683) on pages 8-9 of the Reply, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Simpson discloses that hop acids/resins are bactericidal to several lactobacilli and commercially available source of hop acids for inhibition of growth of lactic acid bacteria such as ISOHOPCO2N. Simpson is relied upon as a teaching of using isomerized hop acids in inhibiting of lactic acid bacteria. As stated in the previous Office Action, Simpson discloses that hop acids present in the brewery yeast slurries have a bacterial action on lactic acid bacteria during the acid washing process (p. 405). Simpson disclose introduction into

microorganisms of aqueous solution of "isomerised hop extract (ISOHOPCO2N, Pauls Hop Products, England) hopped to a level of 60° EBCBU" (p. 406). Simpson also discloses that solution contains 0-85% NaCl (p. 406). Thus Simpson discloses alkaline aqueous solution of isomerized hop acid. Simpson also discloses that alkaline aqueous solution of isomerized hop acid is maintained at 5° C (p. 406). As evidenced by Kaneda et al (Beer Absorption on a Lipid Membrane as Related to Sen Evaluation), the concentration of isomerized acids in ISOHOPCO2N product is 30%, in particular the concentration of isohumulone (isoalpha acid) is 21.6%.

'863 patent discloses a process for isomerizing alpha acids to iso-alpha acids. '863 patent discloses "a process for transforming an alpha acid into an iso-alpha acid, involving contact of the alpha acid with an aqueous solution of a metal ion, comprising the steps of contacting an aqueous solution of the metal ion with a water-immiscible organic solvent solution of the alpha acid under conditions where the alpha acid is dissolved or remains dissolved in said organic solvent and effecting the desired isomerization in the water-immiscible organic solvent with or without prior separation of said solvent containing said alpha acid from the aqueous phase, having numerous advantages over the prior art as herein elsewhere set forth" (Col. 4 lines 10-22). '863 patent discloses "the pH of any water phase is above 8.0 and preferably 13 or below and the temperature is below 50°C" (Col. 4 lines 31-33). '863 patent discloses "metal ions are introduced into the said hop extract while the solvent is present, the mixture held until isomerization occurs, and the solvent removed; metal ions are removed by washing the said hop extract contained in the solvent with dilute acid prior to removal of



the solvent; the said mixture is held at a temperature below 50°C until isomerization occurs" (Col. 4 lines 40-47). '863 patent teaches the following advantages of the disclosed method: it eliminates the need to remove the solvent from the extract prior to isomerization; it permits continuous processing of the hops, from extraction to isomerization to solvent removal, without intermediate heating and cooling of the solvent; it permits the isomerization to be conducted at an increased rate, under conditions which eliminate the hazard of oxidation, hydrolysis, and further isomerization of the iso-alpha acids; it eliminates the necessity for carefully controlled amounts of reagents which, combined with mild conditions, makes the reaction foolproof; it greatly reduces the size and volume of equipment required to process a given quantity of hops, because the concentration of extract in the water-immiscible solvent is not critical, and may in the process of this invention be very high (Col. 10 lines 50-68).

Since Simpson discloses that hop acids have a bacterial action on lactic acid bacteria and adding aqueous isoalpa acid alkaline solution to yeast, and '863 Patent teaches a process for isomerizing alpha acids to iso-alpha acids, it would have been obvious to modify combined teachings of Todd, Jr. et al. and Simpson and employ a method of preparation of aqueous alkaline hop acid solution in order to obtain aqueous isoalpa acid alkaline solution with all the commercial advantages listed above as taught by '863 Patent.

### ***Conclusion***

**THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to VERA STULII whose telephone number is (571)272-3221. The examiner can normally be reached on 7:00 am-3:30 pm, Monday-Friday.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Keith Hendricks can be reached on (571) 272-1401. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Steve Weinstein/  
Primary Examiner, Art Unit 1794

/Vera Stulii/  
Examiner, Art Unit 1794